PROFESSIONAL INFORMATION

SCHEDULING STATUS:

S2

1. NAME OF THE MEDICINE

ADCO FLUPAIN

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each 5 ml contains:	
Triprolidine hydrochloride	0,625 mg
Pseudoephedrine hydrochloride	15 mg
Paracetamol	125 mg

Preservatives: Methylparaben 0,12 % $^{m}/_{v}$ and Propylparaben 0,02 % $^{m}/_{v}$

Contains alcohol: 0,5 % $^{v}/_{v}$

Contains sweetener: Saccharine Sodium 0,01 g and 1,5 g 70 % sorbitol solution

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Syrup

A clear, pink to red syrup with a raspberry odour.

4. CLINICAL PARTICULARS

4.1 Therapeutic Indications

For the relief of symptoms such as nasal congestion, sniffing and headache associated with the common cold and influenza.

4.2 Posology and method of administration

Children 2 to 5 years: 5 ml three times daily

Children 6 to 12 years: 5 ml to 10 ml three times daily

Not for use in children under 2 years of age (See section 4.4)

Do not use continuously for longer than 10 days without consulting your doctor.

Consult your doctor if no relief is obtained with the recommended dosage.

DO NOT EXCEED THE RECOMMENDED DOSE

Method of administration: Oral administration only.

4.3 Contraindications

- Hypersensitivity to triprolidine hydrochloride, pseudoephedrine hydrochloride, paracetamol or to any of the excipients listed in section 6.1
- Cardiovascular disease (especially coronary insufficiency)
- Severe hypertension or uncontrolled hypertension
- Thyrotoxicosis
- Prostatism
- Bladder dysfunction
- Narrow angle glaucoma
- Pheochromocytoma
- In patients being treated with monoamine oxidase inhibitors and within two weeks of stopping such treatment as a hypertensive response may result.
- Do not use in children under 2 years of age.
- During an attack of asthma.
- Avoid during halogenated anaesthesia.
- Severe acute or chronic kidney disease/ renal failure

4.4 Special warnings and precautions for use

ADCO FLUPAIN contains paracetamol which may be fatal in overdose. In the event of overdosage or suspected overdose and notwithstanding the fact that the person may be asymptomatic, the nearest doctor, hospital or Poison Control Centre must be contacted immediatelv.

- ADCO FLUPAIN contains paracetamol. Dosages of ADCO FLUPAIN in excess of those recommended may cause severe liver damage. Consult a medical practitioner if pain or fever persists or gets worse at the recommended dosage, if new symptoms occur or if redness and swelling is present, as these could be signs of a more serious condition.
- Contains glycerol and may have a laxative effect.
- Sorbitol may cause gastrointestinal discomfort and mild laxative effect
- Patients with the rare hereditary condition of sorbitol intolerance should not take ADCO FLUPAIN.
- hyperthyroidism
- diabetes mellitus
- severe hepatic impairment.
- The additive effect of concomitantly administered products containing sorbitol (or fructose) and dietary intake of sorbitol (or fructose) should be taken into account. The content of sorbitol in medicinal products for oral use may affect the bioavailability of other medicinal products for oral use administered concomitantly.
- Severe cutaneous adverse reactions (SCARs) such as toxic epidermal necrolysis (TEN), Steven-Johnson syndrome (SJS), acute generalized exanthematous pustulosis (AGEP), drug reaction with eosinophilia and systemic symptoms (DRESS)/ Drug-induced hypersensitivity syndrome (DIHS) and fixed drug eruptions (FDE) have been reported in patients treated with paracetamol containing medicines. If a patient develops SCAR, treatment with ADCO FLUPAIN must immediately be discontinued and appropriate treatment instituted (see Section 4.8).
- Posterior reversible encephalopathy syndrome (PRES) and reversible cerebral vasoconstriction syndrome (RCVS). Cases of PRES and RCVS have been reported with the use of pseudoephedrine-containing products (see section 4.8). The risk is increased in patients with severe or uncontrolled hypertension, or with severe acute or chronic kidney disease/renal failure

(see section 4.3). Pseudoephedrine should be discontinued and immediate medical assistance sought if the following symptoms occur: sudden severe headache or thunderclap headache, nausea, vomiting, confusion, seizures and/or visual disturbances. Most reported cases of PRES and RCVS resolved following discontinuation and appropriate treatment.

4.5 Interaction with other medicines and other forms of interaction

Interactions with other medicines

- ADCO FLUPAIN should be used with caution in patients taking other *sympathomimetic agents, such as decongestants, appetite suppressants* and *amphetamine-like psychostimulants, or antihypertensive agents*, as this may cause a rise in blood pressure largely because of interaction with pseudoephedrine HCl. The effects of a single dose of ADCO FLUPAIN on the blood pressure of patients should be observed before recommending repeated or unsupervised treatment.
- The antibacterial agent, *furazolidone*, is known to cause a dose-related inhibition of monoamine oxidase. ADCO FLUPAIN and furazolidone should not be taken together.
- The effects of ADCO FLUPAIN due to pseudoephedrine HCl, are diminished by *guanethidine, reserpine, methyldopa* and may be diminished by *tricyclic antidrepressants*. The effects of atropine and tricyclic antidepressants may be enhanced by triprolidine HCl.
- Triprolidine HCl may mask the warning symptoms of damage caused by *ototoxic ~~drugs~~ <u>medicines</u>* and may affect the metabolism of ~~drugs~~ <u>medicines</u> in the liver.
- Long term use of *anticonvulsants* and *oral steroid contraceptives* cause an increase in the first past metabolism or clearance rate and may prevent attainment of therapeutic levels. Reversal of the effect of antihypertensive agents may occur.
- Do not give together with *cardiac glycosides, quinidine*, and *tricyclic antidepressant* medicines.
- The depressant effects of triprolidine are aggravated by *alcohol, anaesthetics*, *hypnotics, sedatives, tricyclic antidepressants and phenothiazines*.
- *Monoamine oxidase inhibitors* may enhance the anticholinergic effects.
- Pseudoephedrine may partially reverse the hypotensive action of medicines which interfere with sympathetic activity including *bretylium, bethanidine, guanethidine*, *debrisoquine and methyldopa.*

- Pseudoephedrine should be avoided or used with caution in patients undergoing *anaesthesia with cyclopropane, halothane or other halogenated anaesthetics* as they may induce ventricular fibrillation.
- *Metoclopramide* - Absorption of ADCO FLUPAIN may be accelerated.
- *Cholestyramine* - Absorption of ADCO FLUPAIN is reduced if given within one hour of cholestyramine
- Prolonged concurrent use of with *salicylates* increases the risk of adverse renal Effects
- *Warfarin and Anticoagulants*- concurrent, chronic, high-dose administration of ADCO FLUPAIN may increase the anticoagulant effect. Paracetamol is recommended as the general analgesic and antipyretic of choice in patients on oral anticoagulant therapy.
- *Antiepileptics*: The plasma-paracetamol concentrations considered an indication for antidote treatment should be halved in patients receiving enzyme inducing medicines such as *carbamazepine, phenobarbital, phenytoin, or primidone*.
- *Probenecid*: Pre-treatment with probenecid can decrease paracetamol clearance and increase its plasma half-life. Although urinary excretion of the sulphate and glucuronide conjugates of paracetamol are reduced, that of paracetamol is unchanged.
- Antibacterials: The plasma-paracetamol concentrations considered an indication for antidote treatment should be halved in patients receiving enzyme inducing medicines such as rifampicin. Severe hepatotoxicity at therapeutic doses or moderate overdoses of paracetamol has been reported in patients receiving isoniazid, alone or with other medicines for tuberculosis.
- Antivirals: Severe hepatotoxicity has occurred after use of paracetamol in a patient taking zidovudine and co-trimoxazole. However, neither short-term nor long-term studies (the latter also in an individual patient) have shown any alteration of zidovudine elimination in patients taking zidovudine and paracetamol. Paracetamol has also been found to enhance the antiviral effect of interferon alfa.

4.6 Fertility, pregnancy and lactation

Do not take this product during pregnancy or whilst breastfeeding.

No fertility data available

4.7 Effects on ability to drive and use machines

ADCO FLUPAIN may lead to drowsiness and impaired concentration that may be aggravated by simultaneous intake of alcohol or other central nervous system depressants. Patients should be warned that their child's concentration may be impaired.

4.8 Undesirable effects

System Organ Class	*Frequency*	*Undesirable effect*
Blood and lymphatic system disorders	Less frequent	Thrombocytopenia, agranulocytosis, leucopoenia, neutropenia, pancytopenia, haemolytic anaemia
Immune system disorders	Less frequent	Allergic reactions, hypersensitivity – cross sensitivity may occur with other sympathomimetics
	Unknown	Anaphylaxis, rashes, photosensitivity, drug-induced hypersensitivity syndrome (DIHS) (hypersensitivity reactions characterised by urticaria, dyspnoea, and hypotension) (see Section 4.4).
Endocrine disorders	Unknown	Hair loss
Metabolism and nutrition disorders	Unknown	Pyroglutamic aciduria (5-oxoprolinuria), high-anion gap metabolic acidosis, reduced appetite, altered metabolism, disturbances of glucose metabolism
Psychiatric disorders	Frequent	Restlessness, insomnia, nervousness
	Less frequent	Hallucination, confusional state, depression
	Unknown	anxiety, paraesthesia, fear, irritability, psychotic state, agitation, delusion, euphoric mood
Nervous system disorders	Frequent	CNS depression ranging from slight drowsiness to deep sleep, dizziness, incoordination (paradoxical stimulation may occur in children), headache, psychomotor impairment
	Less frequent	convulsions, myalgia, tremor, extrapyramidal effects
	Unknown	Cerebrovascular accident, posterior reversible encephalopathy syndrome (PRES) (see section 4.4), reversible cerebral vasoconstriction syndrome (RCVS) (see section 4.4)
Eye Disorders	Frequent	Vision blurred
	Unknown	Ischaemic optic neuropathy
Ear and labyrinth disorders	Unknown	Hearing loss, tinnitus

Cardiac disorders	Less frequent	Palpitations, dizziness, fainting, tachycardia, reflex bradycardia, dysrhythmias, cardiac arrest, dyspnoea
	Unknown	Possible increase in the risk of hypertension, anginal pain, cardiac oedema
Vascular disorders	Less frequent	Sweating, hypotension
	Unknown	Vasoconstriction with resultant hypertension, cerebral haemorrhage
Respiratory, thoracic and mediastinal disorders	Frequent	Thickened respiratory tract secretions
	Less frequent	Bronchospasm
	Unknown	Pulmonary oedema, dry throat, epistaxis, nasal dryness
Gastrointestinal disorders	Frequent	Dry mouth, constipation, increased gastric reflux, nausea
	Less frequent	Vomiting, diarrhoea, epigastric pain, Pancreatitis,
	Unknown	Hypersalivation, ischaemic colitis
Hepatobiliary disorders	Less frequent	Hepatitis
Skin and subcutaneous tissue disorders	Less frequent	Skin rash (usually erythematous or urticarial), Dermatitis, and other allergic reactions such as Stevens Johnson Syndrome (SJS), Toxic Epidermal Necrolysis (TEN), Acute Generalised Exanthematous Pustulosis (AGEP). The rash is usually erythematous or urticarial but sometimes more serious and accompanied by fever and mucosal lesions. More mild rashes and other hypersensitivity reactions also occur Occasionally, pruritus
	Unknown	Fixed drug eruptions (FDE) (see Section 4.4).
Renal and urinary disorders	Frequent	Urinary retention
	Less frequent	Renal colic, renal failure and sterile pyuria, difficulty in micturition
	Unknown	Nephropathy, dysuria
General disorders and administrative site conditions	Unknown	Weakness, fatigue, hyperpyrexia

Reporting of suspected adverse reactions

Reporting suspected adverse reactions after authorisation of the medicine is important. It allows continued monitoring of the benefit /risk balance of the medicine. Healthcare Providers are asked to report any suspected adverse reactions to SAHPRA via Med Safety APP (Medsafety X SAHPRA) or via the eReporting platform (who-umc.org) found on the SAHPRA website. Alternatively use the "6.04 Adverse Drug Reactions (ADR)/Product Quality Problem Reporting Form" found online under SAHPRA's publications: https://www.sahpra.org.za/document/adverse-drug-reactions-and-quality-problem-reporting-form/.

Adverse Drug Reactions may also be reported to Adcock Ingram Limited using the following email: Adcock.AEReports@adcock.com

4.9 Overdose

Paracetamol:

Prompt treatment is essential. In the event of an overdosage, consult a doctor immediately, or take the person to a hospital directly. A delay in starting treatment may mean that antidote is given too late to be effective. Evidence of liver damage is often delayed until after the time for effective treatment has lapsed.

Susceptibility to paracetamol toxicity is increased in patients who have taken repeated high doses (greater than 5 -10 g/day) of paracetamol for several days, in chronic alcoholism, chronic liver disease, AIDS, malnutrition, and with the use of medicines that induce liver microsomal oxidation such as barbiturates, isoniazid, rifampicin, phenytoin and carbamazepine.

Symptoms of paracetamol overdosage in the first 24 hours include pallor, nausea, vomiting, anorexia and possibly abdominal pain. Mild symptoms during the first two days of acute poisoning do not reflect the potential seriousness of the overdosage. Liver damage may become apparent 12 to 48 hours, or later after ingestion, initially by elevation of the serum transaminase and lactic dehydrogenase activity, increased serum bilirubin concentration and prolongation of the prothrombin time. Liver damage may lead to encephalopathy, coma and death.

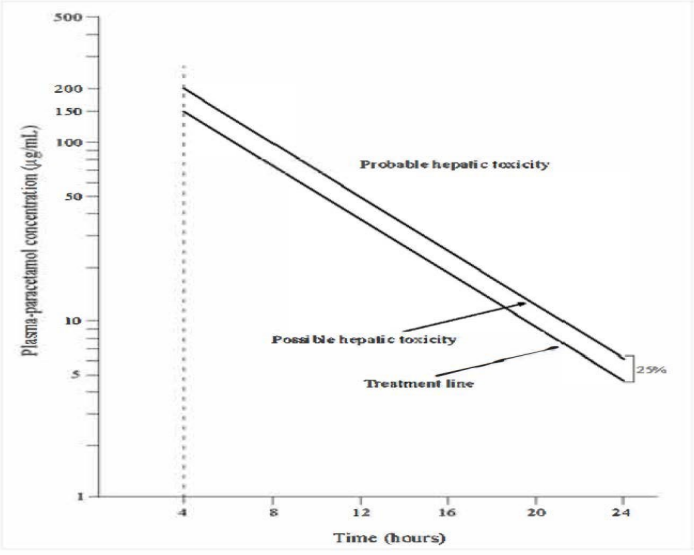
Acute renal failure with acute tubular necrosis may develop even in the absence of severe liver damage. Abnormalities of glucose metabolism and metabolic acidosis may occur. Cardiac dysrhythmias have been reported.

Treatment for paracetamol overdosage:

N-acetylcysteine should be administered to all cases of suspected overdose as soon as possible preferably within eight hours of overdosage, although treatment up to 36 hours after ingestion may still be of benefit, especially if more than 150 mg/kg of paracetamol was taken. An initial dose of 150 mg/kg N-acetylcysteine in 200 ml given intravenously over 15 minutes, followed by an infusion of 50 mg/kg in 500 ml dextrose injection over the next four hours, and then 100 mg/kg in 1000 ml dextrose injection over the next sixteen hours. The volume of intravenous fluid should be modified for children.

Although the oral formulation is not the treatment of choice, 140 mg/kg dissolved in water may be administered initially, followed by 70 mg/kg every four hours for seventeen doses.

A plasma paracetamol level should be determined four hours after ingestion in all cases of suspected overdosage. Levels done before four hours, unless high, may be misleading. Patients at risk of liver damage, and hence requiring continued treatment with N-acetylcysteine, can be identified according to their plasma paracetamol level. The plasma paracetamol level can be plotted against time since ingestion in the nomogram below.



Reference: Martindale: The Complete Drug Reference

Those whose plasma paracetamol levels are above the “normal treatment line”, should continue N-acetylcysteine treatment with 100 mg/ kg IV over 16 hours repeatedly until recovery. Patients with increased susceptibility to liver damage as identified above, should continue treatment if concentrations

are above the “high risk treatment line”. Prothrombin index correlates best with survival. Monitor all patients with significant ingestions for at least ninety-six hours.

Pseudoephedrine HCl:

Symptoms of pseudoephedrine HCl overdosage may include paranoid psychosis, delusions and hallucinations. Treatment is symptomatic and supportive.

Tripolidine HCl:

Overdosage due to triprolidine may be fatal, especially in children in whom the main symptoms are central nervous system stimulation and antimuscarinic effects: ataxia, excitement, hallucinations, muscle tremor, convulsions, dilated pupils, dry mouth, flushed face and hyperpyrexia. Deepening coma, cardiorespiratory collapse and death may occur within 18 hours. In adults, the usual symptoms of overdosage are drowsiness, coma and convulsions. Weakness, dizziness, incoordination, difficulty with micturition, respiratory depression, hypotension, agitation, irritability, hypertension, palpitations, restlessness and tachycardia, may occur. Treatment is symptomatic and supportive.

5. PHARMACOLOGICAL PROPERTIES

A 5.8. Medicines affecting autonomic functions - Preparations for the common cold including nasal decongestants and antihistaminics

Pharmacotherapeutic group: Sympathomimetics, pseudoephedrine, combinations

ATC code: R01BA52

5.1 Pharmacodynamics properties

ADCO FLUPAIN has decongestive, antipyretic, antihistamine and analgesic properties.

5.2 Pharmacokinetic properties

Triprolidine is metabolised after absorption from the gastro-intestinal tract. The half-life of triprolidine varies from 3 to 5 hours. A carboxylated derivative accounts for about half the dose excreted in the urine.

Pseudoephedrine is readily absorbed from the gastrointestinal tract. It is excreted largely unchanged in the urine with small amounts of its hepatic metabolite. It has a half-life of about 5 to 8 hours.

Paracetamol is rapidly and almost completely absorbed following oral administration. Peak plasma concentrations occur within 30 to 60 minutes and the half-life in plasma is about 2 hours after therapeutic doses. Paracetamol is distributed relatively uniformly throughout all body fluids. Approximately 90 – 95% of the dose is metabolized in the liver, primarily by conjugation.

5.3 Preclinical safety data

No data available.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

- Citric acid anhydrous [E330]
- Colour raspberry red H1277 Bba
- Flavour raspberry 203580
- Glycerol [E422]
- Methylparaben [E218]
- Polyvinylpyrrolidone K25
- Propylene glycol
- Propylparaben [E216]
- Saccharin sodium [E954]
- Sodium citrate dihydrate [E331]
- Sorbitol 70 % solution [E420]
- Xanthan gum

6.2 Incompatibilities

No information available.

6.3 Shelf life

24 months.

6.4 Special precautions for storage

Store in safe place, at or below 25 °C..

Protect from light

6.5 Nature and contents of container

Amber glass bottles containing 50 ml, 100 ml, 200 ml and amber PET bottle containing 100 ml

Not all pack sizes may be marketed at the same time.

6.6 Special precautions for disposal

Not applicable.

7. HOLDER OF CERTIFICATE OF REGISTRATION

Adcock Ingram Limited

1 New Road,

Erand Gardens,

Midrand,

1685

Customer Care: 0860 ADCOCK (232625)

8. REGISTRATION NUMBERS:

27/5.8/0260

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

10 June 1993

10. DATE OF REVISION OF THE TEXT

29 May 2025